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The effect of rehabilitation in patients with facioscapulohumeral muscular dystrophy: A prospective clinical study

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Abstract
Aim: Facioscapulohumeral muscular dystrophy (FSHD) is a rare and slowly progressive disease that causes physical limitations. In our study, it was aimed to reveal the effects of rehabilitation and treatment programs applied in FSHMD patients on activities of daily living and walking.
Material and Methods: A clinical intervention trial was conducted. Data of 33 of the 38 patients diagnosed with FSHD were analyzed. A 20-weeks rehabilitation program composed of exercises (muscle-strengthening, stretching, range of motion, balance, coordination, walking, posture, and breathing), patient and family education, and neuromuscular electrical stimulation. Functional assessments were performed with the Barthel-Index (BI), the functional categories of ambulation (FAC) test, and the Oxford muscle strength grading scale before and after the rehabilitation.
Results: Average age of the participants (±SD) was 30.88±11.43 years, and 81.8% (n=27) were males. All patients had periscapular weakness and wing scapula. There was no prominent difference between flexion and extension and abduction of the two upper limb extremities ($p > 0.05$). There was a substantial increase in Barthel scores of the patients after rehabilitation ($Z = 3,535$; $p<0.001$).
Discussion: The implementation of the rehabilitation program causes an increase in BI scores. It is recommended that training of the society and health personnel will be beneficial. Further studies are needed to provide information about the frequency of this disease in the Turkish population.

Keywords
Rehabilitation, Muscular Dystrophy, Activities of Daily Living, Disability Studies, Genetic Disorders

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Introduction

Facioscapulohumeral muscular dystrophy (FSHD) is a rare and unique muscular dystrophy that initially involves the upper region and gradually spreads to the lower region, except for the extraocular and deltoid muscles [1]. A worldwide prevalence study of FSHD found that it ranged from 2.03 to 6.8 per 100,000 live-born [2].

FSHD is a progressive disease that makes daily life addictive. This condition, which initially shows involvement in the face, shoulder circumference, and arm muscles close to the shoulders, progresses towards the abdomen and lower extremities over time, the involvement is typically asymmetrical, weakness and atrophy are observed in the affected areas [3]. Symptoms and deformities such as poly-hill, Beevor's sign, advanced hyperlordosis, Trendelenburg gait, and drop foot occur in the hamstring and posterior calf muscles atrophy [4].

There is still no specific treatment option for FSHD. In these cases, supportive care and extensive rehabilitation are potentially effective in reducing fatigue, cardiorespiratory and muscle atrophy [5,6], and exercise plays an important potential role in preventing fatigue and limiting muscle atrophy, cardiorespiratory deterioration, and metabolic deterioration. However, few studies of aerobic training [5,7,8] and strength training [6,8] have been conducted in FSHD patients. There is no study evaluating the benefits of rehabilitation programs, daily life, and walking in FSHD patients in Turkey. In these patients, it gradually worsens over the years and weakens the lower extremity muscles, making it difficult to walk, and over time, they depend on a caregiver in daily life.

This study aimed to reveal the effects of rehabilitation and treatment programs in FSHMD patients on activities of daily living and walking.

Material and Methods

Our study was conducted as a prospective study on patients diagnosed with FSHD who came to the Center for Neuromuscular Diseases of the Department of Physical Medicine and Rehabilitation, Gazi Yaşargil Training and Research Hospital, University of Health Sciences. The study protocol was approved by the Local Ethics Committee No:809. Each participant signed an informed consent form per the Declaration of Helsinki. The rehabilitation program started after approval.

A total of 38 patients were diagnosed with FSHD in the Neuromuscular Diseases Center. All individuals diagnosed with FSHD were recommended to participate in the study. Three people who did not agree to participate in the study and 2 patients whose questionnaires were deemed invalid were excluded. The results of 33 participants were analyzed.

In this study, we aimed to evaluate the change in BI and FAC values at the beginning and after the active rehabilitation program in FSDH, a genetic muscle disease, and to see the validity of BI and FAC, which are frequently used in rehabilitation in these patients.

The data were obtained through face-to-face interview using a questionnaire by the researcher. Demographic and clinical information was collected using the sociodemographic data form created by the researchers after reviewing the current literature. The independent variable of the study was the rehabilitation program, and the dependent variables were the extremity muscle strength, Barthel-Index (BI) and Functional Ambulation Classification (FAC) scores of the patients.

Since FSHD physical and neurological manifestations may be different, a personalized rehabilitation program was prepared for each patient, taking into account the individual's mental, fatigue and participation desire, not exceeding daily 1 hour. The rehabilitation program consisted of 5 days per week for 20 weeks. Ankle orthoses were fitted to patients with ankle dorsiflexion loss and associated walking difficulties.

Functional assessment tools are described below.

As a prospective study, to see the use of BI and FAC in patients with FSDH, to prevent musculoskeletal disorders and neurological losses, and to implement rehabilitation to keep walking and daily life independent.

Barthel-Index:

Barthel's index of activities of daily living (BI) was first developed by Mahoney and Barthel [9]. The validity and reliability of the Turkish version of the BI were performed by Küçükdeveci et al [10]. BI is a life activity scale consisting of 10 basic parameters commonly used in physical disability. These 10 parameters are feeding, bathing, personal care, dressing, bowel management, bladder management, toilet use, wheelchair use, walking on level ground, and climbing stairs. Each point determines the degree of physical assistance and the amount of time a person needs to perform the independent activity. Points are given to the activities performed by the patient. A score of 100 is considered completely independent, and a score of zero is considered completely dependent.

Functional Ambulation Classification:

The functional categories of ambulation (FAC) test was developed by Holden et al. in 1984 to determine the level of ambulation [11]. FAC is a scale with six categories (0-5); the lowest stage means more addiction. Stages 0 to 3 indicate that the patient is dependent, or stages 4 and 5, in which you are not standing, are independent.

Oxford Muscle Strength Grading Scale:

This is a muscle strength measurement technique. The force exerted by a person against the resistance on the right axis during the movement is scored between zero and 5; 0/5: no muscle strength, 1/5: if gravity is removed, there is only contraction; 2/5: completes the movement when gravity is removed; 3/5: it only completes anti-gravity motion, with no resistance; 4/5: muscle activation against some resistance; 5/5: muscle activation to examiner full resistance, full range of motion [12].

Those who accepted to participate in the survey were briefed about the research and no identifying information was recorded in the survey. The data collection processes of the participants and the examination were carried out by the same researcher. Error checking was done after the data were entered into the computer.

The data were entered into the computer using SPSS 20.0 software. Descriptive statistics were done to present participant characteristics by summarizing in percentages for categorical variables and as mean ± standard deviations (SD) or median and inter-quartile range (IQR) for numerical variables. Comparison of right and left side muscle strength was made

using the Wilcoxon signed-ranks test. Comparison of Barthel and FAC scores before and after rehabilitation was made using the Wilcoxon signed-rank test. A p-value of <0.05 was considered statistically significant.

Results

The study comprised 33 patients with FSHMD. The mean (±SD) age of the participants was 30.88±11.43 years, and 81.8% (n=27) were male. The male/female ratio was 4.5. The mean (±SD) delay between diagnosis and the onset of symptoms was 7.40 ± 8.79 years. The mean value (±SD) of the body mass index (BMI) was 21.40±3.44. Of the patients, 72.7% (n = 27) had a family history of the disease, and parents of 60.6% (n = 20) of the patients had consanguineous marriages. Basic characteristics variables of patients are given in Table 1.

The most common symptoms were periscapular weakness (100.0%; n = 33), winged scapula (100.0%; n = 33), dysphonia (66.7%; n = 23) and facial muscle weakness (63.6%; n = 21), respectively. Two patients were not able to walk (Table 2).

There was no visible difference between the right and left flexion and extension and abduction muscle strengths of the lower and upper limb (p> 0.05), except hip abduction and extension (p<0.05) (Table 3).

There was no prominent difference between the two shoulder flexion, abduction, and extension muscle strengths in patients with and without dysphonia. (p> 0.05).

There was a significant increase in the Barthel scores of the patients after rehabilitation (median= 75.0; IQR= 20.0) compared to before (median=80.0; IQR=15.0) (Wilcoxon Z= 3.535; p<0.001) (Figure 1).

There was no statistically prominent difference between the FAC scores of FSHMD patients before (median= 4.0; IQR=2.0) and after (median=4.0; IQR=1.5) rehabilitation (Z=1.732; p=0.083).

Compared to the values before rehabilitation (median= 70.0; IQR=3.75), Barthel scores of the patients using ankle-foot-orthotics increased significantly after rehabilitation (median= 85.0; IQR=3.75) (Z=2.459; p= 0.014). However, compared to the levels before rehabilitation (median= 3.5; IQR=1.0), there was a borderline significant increase in the FAC scores after rehabilitation (median= 4.0; IQR=0.0) (Z=1.732; p= 0.087).

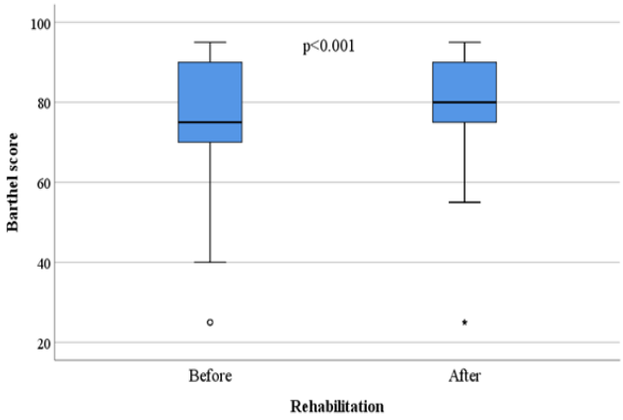

Figure 1. Barthel scores of FSHMD patients before and after rehabilitation.

Table 1. FSHD patients' basic characteristics

		Mean / n	SD / %
Age (years)		30.88	11.43
Gender	Female	6	18.2
	Male	27	81.8
Age at diagnosis (years)		20.85	8.74
Symptoms onset age (years)		13.45	6.2
Height (cm)		167.48	13.39
Weight (kg)		60.06	13.63
BMI		21.40	3.44
Smoking	Currently using	13	39.4
	Used in the past	5	15.
	Never smoked	15	45.5
Family history of the disease	Yes	24	72.7
	No	9	27.3
Number of siblings		7.55	2.17
Consanguineous parents	No	20	60.6
	Yes	13	39.4

SD: Standard deviation

Table 2. Clinical characteristics of the patients

	No		Yes	
	n	%	n	%
Periscapular weakness	0	0.0	33	100.0
Winged scapula	0	0.0	33	100.0
Dysphonia	11	33.3	22	66.7
Facial muscle weakness	12	36.4	21	63.6
Increased thoracic kyphosis	19	57.6	14	42.4
Increased lumbar lordosis	21	63.6	12	36.4
Dysarthria	22	66.7	11	33.3
Facial asymmetry	22	66.7	11	33.3
Posture disorder	23	69.7	10	30.3
Ability to walk	2	6.1	31	93.9

Table 3. Comparison of patients' right and left side muscle strengths

	Right side		Left side		Z	p
	Median	IQR	Median	IQR		
Shoulder flexion	3.00	2.00	3.00	1.00	1.698	0.090
Shoulder abduction	3.00	2.00	3.00	2.00	1.604	0.109
Shoulder extension	3.00	2.00	3.00	2.00	1.147	0.251
Elbow flexion	3.00	1.00	3.00	1.00	1.155	0.248
Elbow extension	3.00	1.00	3.00	1.00	0.905	0.366
Wrist extension	4.00	1.00	4.00	0.00	0.905	0.366
Wrist flexion	4.00	0.00	4.00	0.00	0.816	0.414
Handshake	4.00	1.00	4.00	1.00	0.577	0.564
Hip flexion	4.00	1.00	4.00	1.00	0.707	0.480
Hip abduction	4.00	1.00	4.00	1.00	2.070	0.038
Hip extension	3.00	2.00	3.00	1.00	2.126	0.033
Knee flexion	4.00	1.00	4.00	1.00	0.000	1.000
Knee extension	4.00	1.00	4.00	1.00	0.632	0.527
Ankle dorsal flexion	4.00	2.00	4.00	2.00	0.318	0.751
plantarflexion	4.00	1.00	4.00	1.00	0.359	0.719

IQR: Interquartile range, Z: Wilcoxon signed ranks test value

Discussion

The majority of FSHMD patients were male. There was approximately 7 years of delay between the onset of the symptoms and the diagnosis. Family history and consanguineous marriages between the parents were common in the patients. The most common symptoms were periscapular weakness, winged scapula, dysphonia, and facial muscle weakness. However, there was an increase in the BI scores after rehabilitation.

Due to ethical concerns, a control group could not be used in the study. Although all potential participants were invited, the study had a relatively low sample size due to the extremely rare nature of the disease. Genealogical analysis, although not among the study objectives, could provide further information about the genetic dimension of the disease

Symptom onset in FSHD patients may occur throughout the entire life span, but it is reported most frequently in the second decade of life [1,13]. The age of onset of symptoms in our study was similar to that reported in the literature. FSHD has less severe progress in females than males and is diagnosed at a more advanced age than in males [2]. This explains why the ratio of men to women is higher in favor of men in our study.

An important problem is that it is diagnosed years after the onset of symptoms. Thus, there is a need for raising awareness about this disease, both at the social and at the health employee level.

Two types of FSHD have been identified that are inherited in an autosomal dominant manner FSHD1 (95% of those affected) and FSHD2. Although both types have different genetic causes, their symptoms and signs are the same. FSHD1 is caused by abnormal expression of the DUX4 gene located in the D4Z4 region of chromosome 4, while in FSHD2, there is a mutation in the D4Z4 region of the SMCHD1 gene [14]. In a study by Wohlgemuth et al., the proportion of symptomatic mutation carriers was 58% [15]. However, the high proportions of consanguineous marriages may have contributed to the high family history in our study.

In preparing for clinical trials and improving clinical care, it is crucial to understand what symptoms are most frequently experienced and essential to patients with FSHD [16]. A study by Hamel et al reported losses mostly in the shoulders or arms (96.9%) and limitations in activities (94.7%), core weakness (93.8%), and fatigue (93.8%) [17]. In the upper extremities, the muscles that fix and hold the scapula the scapular, especially the trapezius and serratus anterior, are frequently involved. This is the result of FSHD with asymmetrical, bilaterally involved scapular blades affecting the BI [18]. Symptoms, such as periscapular weakness, winged scapula, and facial muscle weakness we detected in our study are compatible with the literature. Since facial muscle weakness is not evident at the beginning of FSHD, symptoms of limited lip movements such as keeping eyes open while sleeping, using a straw, and whistling can be seen. Normally, a difference in strength loss is expected between the two extremities. In our cases, it may be due to the patient's inability to cooperate during the measurement and the lack of sensitivity of the measurement technique. However, if digital myometers were used instead of manual measurement to enable a more precise measurement of muscle strength, a significant observation could be confirmed. Winged scapula can also be seen in other muscle diseases, but they are affected asymmetrically.

In many studies, FSHD has not found any pharmacological evidence that preserves strength and slows muscle loss, and it has been found to be effective in maintaining functional status in terms of scapula fixation, individualized, different-intensity strengthening, aerobic exercises, since the diagnosis [19]. A few studies have worked towards the treatment of physical limitations and fatigue symptoms, aerobic exercise has succeeded in relieving chronic fatigue and increasing physical activity and fitness [7].

In 2016, at-home clinical trial of exercise therapy for FSHD patients investigated the benefit of combined aerobic and strength programs. The results showed that individuals participating in a 6-month program had significantly improved muscle function without further damage to their diseased tissues [6]. In severe pathological conditions, a physical and rehabilitation program alone may not be sufficient for treatment to correct functional limitations. Therefore, assistive devices can be used to add BI and FAC according to the specific therapeutic needs of each patient. The disease can be partially restored using low ankle-foot-orthoses or knee-ankle-foot orthoses [20].

When we measured the BI and FAC values on the first and last day of the rehabilitation process, we found a significant positive change in the values of the patients who were taken into active rehabilitation. We applied an ankle orthosis to those with walking potential and severe drop foot. We saw a significant increase in BI and FAC values.

In the evaluation made at the end of the program, it was observed that although there was no significant increase in muscle strength, the proportions of balance loss and falling decreased considerably, and there was an improvement in daily living activities and walking. This was mostly attributed to not motivating the patients, disuse atrophy, and loss of strength. Although we focused more on strengthening, it was seen that when considered on a patient basis, each exercise was effective and beneficial separately.

Conclusion

Since there is no definitive treatment for FSHM, the effectiveness of rehabilitation is expressed in every piece of information, but a standard program has not been established so far. Other scales can be developed to better measure the effectiveness of rehabilitation, and we concluded that the BI and FAC scales are easy to apply and can be used in the rehabilitation program of these patients. Additionally, since the disease is genetically inherited, patients should be directed to genetic counseling for information about the risk of genetic transmission. Since the condition is not known enough both in the community and among the primary health care personnel, it is diagnosed late. Therefore, we believe that training of the society and health personnel will be beneficial. Besides, further studies are needed to provide information about the frequency of this disease in the Turkish population.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some

of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest
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References
1. Tawil R. Facioscapulohumeral muscular dystrophy. Handb Clin Neurol. 2018;148: 541-8.
2. Statland JM, Tawil R. Facioscapulohumeral Muscular Dystrophy. Continuum: (Minneap Minn). 2016; 22(6):1916–31.
3. Lin XD, He JJ, Lin F, Chen HZ, Xu LQ, Hu W, et al. A "triple trouble" case of facioscapulohumeral muscular dystrophy accompanied by peripheral neuropathy and myoclonic epilepsy. Chin Med J. 2018; 131 (18): 2164-71.
4. Chen TH, Wu YZ, Tseng YH. Early-onset infantile facioscapulohumeral muscular dystrophy: a timely review. Int J Mol Sci. 2020; 21(20):7783.
5. Hamel J, Tawil R. Facioscapulohumeral muscular dystrophy: Update on pathogenesis and future treatments. Neurotherapeutics. 2018;15 (4): 863–71.
6. Bankolé LC, Millet GY, Temesi J, Bachasson D, Ravelojaona M, Wuyam B, et al. Safety and efficacy of a 6-month home-based exercise program in patients with facioscapulohumeral muscular dystrophy A randomized controlled trial. Medicine. 2016; 95(31): 1-10.
7. Andersen G, Prahm KP, Dahlqvist JR, Citirak G, Vissing J. Aerobic training and postexercise protein in facioscapulohumeral muscular dystrophy. Neurology. 2015;85(5):396-403.
8. Faux-Nightingale A, Kulshrestha R, Emery N, Pandyan A, Willis T, Philp F. Upper Limb Rehabilitation in Facioscapulohumeral Muscular Dystrophy: A Patients' Perspective. Arch Rehabil Res Clin Transl. 2021; 3(4): 100157.
9. Barthel D, Mahoney F. Functional evaluation: The Barthel Index. Md State Med J. 1965;14:61-65.
10. Kucukdeveci AA, Yavuzer G, Tennant A, SuSulfur, Sonel B, ArBrazil. Adaptation of the modified Barthel Index for use in physical medicine and rehabilitation in Turkey. Scand J Rehabil Med. 2000;32(2): 87-92.
11. Holden MK, Gill KM, Magliozzi MR, Nathan J, Piehl-Baker L. Clinical gait assessment in the neurologically impaired. Reliability and meaningfulness. Physical Therapy. 1984;64 (1):35–40.
12. Clarkson HM. Musculoskeletal assessment: joint range of motion and manual muscle strength. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2000.
13. Orrell RW. Facioscapulohumeral dystrophy and scapuloperoneal syndromes. Handb Clin Neurol.2011;101:167-80.
14. Johanna H, Tawil R. Facioscapulohumeral muscular dystrophy: Update on pathogenesis and future treatments. Neurotherapeutics. 2018; 15(4): 863–71.
15. Wohlgemuth M, Lemmers RJ, Jonker M, van der Kooi E, Horlings CG, van Egelen BG, et al. A family-based study into penetrance in facioscapulohumeral muscular dystrophy type 1. Neurology. 2018;91(5):e444–54.
16. Bakker M, Schipper K, Geurts AC, Abma TA. It's not just physical: a qualitative study regarding the illness experiences of people with facioscapulohumeral muscular dystrophy. Disabil Rehabil. 2017;39(10):978–86.
17. Hamel J, Johnson N, Tawil R, Dilek N, McDermott MP, Heatwhole C. Patient-reported symptoms in facioscapulohumeral muscular dystrophy (PRISM-FSHD). Neurology. 2019;93(12):e1180–92.
18. Mul K, Lassche S, Voermans NC, Padberg GW, Horlings CG, van Engelen BG. What's in a name? The clinical features of facioscapulohumeral muscular dystrophy. Pract Neurol. 2016;16(3):201–7.
19. Tawil R, Kissel JT, Heatwole C, Pandya S, Gronseth G, Benatar M. Evidence-based guideline summary: Evaluation, diagnosis, and management of facioscapulohumeral muscular dystrophy. Neurology. 2015; 85(4): 357–64.
20. Lu J, Yao Z, Yang Y, Zhang C, Zhang J, Zhang Y. Management strategies in facioscapulohumeral muscular dystrophy. Intractable Rare Dis Res. 2019;8(1):9–13.

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